# JC13 Rec'd PCT/PTO 01 APR 2005

# Sequence Listing SEQUENCE LISTING

<110>	THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES Tsai, Robert Y.L. MCKay, Ronald D.G.	
<120>	METHODS FOR CONTROLLING PROLIFERATION OF CELLS	
<130>	4239-66642	
<150> <151>	PCT/US03/31321 2003-10-01	
<150> <151>	60/442,005 2003-01-22	
<150> <151>	60/415,867 2002-10-02	
<160>	14	
<170>	PatentIn version 3.2	
<210> <211> <212> <213>	1 1810 DNA Rattus rattus	
<220> <221> <222> <223>	misc_feature (1705)(1705) n is a, c, g, or t	
<400> gcggcc	1 gagg tacctgagac ctcttctgct ccagacgcgt ccgcggccag gatgaagagg	60
ccgaag	ttaa agaaagcaag taaacgtatg acctgtcata agcggtataa aatccagaaa	120
aaggtt	cgag aacatcatcg aaaattaagg aaggaagcta aaaagcgggg tcacaagaag	180
cctaag	aagg acccaggagt tccaaatagt gctcccttta aagaggctct tcttcgtgaa	240
gctgag	ctaa ggaaacagca gcttgaagaa ctaaaacagc agcagaaact tgacaggcaa	300
aaagaa	caag aacgaaaaag aaaacttgaa attagccctg atgatgagca atctaatgtg	360
gaaact	cagg aggaatctga tgagcccaaa ataaagaaag ctaaatcagg caaacagaat	420
ccaaag	aagt tacattgtca ggaacttaaa aaggtgattg aagcctcaga cattgtgtta	480
gaagtt	ttgg atgccagaga tcctcttggt tgcaggtgtc ctcaagtaga agaagctgtt	540
atccaa	agtg gatgtaaaaa actagtactt gtattaaata agtcagatct agtaccaaaa	600
gagaat	ctag agaactggct aacttacttg aataaggaat tgccaacagt ggtgttcaaa	660
gcctca	acaa acttaaagaa cagaaagaag acattcaaga taaagaagaa agttgttcca	720
ttccaa	agta aactctgctg tggcaaggaa gcactgtgga agctccttgg aggttttcag	780
	·	

		Sequence I	_istina		
cagtcctgtg gaaaa	ggagt tcaggttgga			gggaaaaagc	840
agcatcatta atagt	ttaaa acaagaaagg	atttgcagtg	ttggagtttc	catgggactt	900
acaaggagta tgcag	attgt ccctttagad	aaacagatca	caatcataga	tagtccgtgc	960
ttcattatct cacct	tgtaa ctcccctgct	gcacttgccc	tccgaagtcc	agcaagtatt	1020
gaagttctaa gacca	ttgga ggctgccagt	gccatcctgt	ctcaggctga	tagtcaacag	1080
gtggtgttaa aatat	actgt cccggggtat	aaggattctc	tggattttt	tactaaactt	1140
gctcagagaa gaggt	ctgca ccaaaaaggt	ggaagcccaa	atgtcgaaag	tgctgctaag	1200
ctgctatggt ctgag	tggac aggtgcctca	ttaggttact	actgccatcc	ccctgcatcc	1260
tggaatcatt ctcct	cattt taatgagaat	attacagcaa	tcatgaagag	gggctttaat	1320
ctagaagaac tagaa	aagaa taatgcacad	agcatacaag	tcctcaaggg	ccctcattta	1380
actaataaaa tcctt	ttccg gtcttcggg	: ctgacaaatg	gaatactaga	agaaaaggac	1440
atccccgaag agtca	ccaaa acagacagaa	gaccaacagg	atggtgatga	tcaagaacat	1500
gttactggtg aaaaa	aatgc agagatctca	gatgtgactc	ctgtagaaga	gaccagggag	1560
atgtcacctg ggcaa	tcaac agcaagtaaa	ı ccatctgaca	gatcctttat	cttggataaa	1620
atgagtgaag aagac	gatgc ctatgactti	accacagatt	atatatagcc	ttctaaatgt	1680
tcaagtgtgc tctgt	acagt gtttntagat	tgctttggta	tgatataaag	tgtaaatctt	1740
gtgaatatgt atcat	gtttt aaattaaaa	ı caaaataaaa	agtgtttgta	taaaaaaaaa	1800
aaaaaaaaa					1810

2 538 <210> <211>

<212> PRT

<213> Rattus rattus

<400> 2

Met Lys Arg Pro Lys Leu Lys Lys Ala Ser Lys Arg Met Thr Cys His 1  $\phantom{000}5\phantom{000}$  10  $\phantom{000}15\phantom{000}$ 

Lys Arg Tyr Lys Ile Gln Lys Lys Val Arg Glu His His Arg Lys Leu  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Arg Lys Glu Ala Lys Lys Arg Gly His Lys Lys Pro Lys Lys Asp Pro 35 40 45

Gly Val Pro Asn Ser Ala Pro Phe Lys Glu Ala Leu Leu Arg Glu Ala 50 60

Glu Leu Arg Lys Gln Gln Leu Glu Glu Leu Lys Gln Gln Gln Lys Leu 65 70 75 80

Asp Arg Gln Lys Glu Gln Glu Arg Lys Arg Lys Leu Glu Ile Ser Pro 85 90 95 Asp Asp Glu Gln Ser Asn Val Glu Thr Gln Glu Glu Ser Asp Glu Pro 100 105 110 Lys Ile Lys Lys Ala Lys Ser Gly Lys Gln Asn Pro Lys Lys Leu His 115 120 125 Cys Gln Glu Leu Lys Lys Val Ile Glu Ala Ser Asp Ile Val Leu Glu 130 135 140 Val Leu Asp Ala Arg Asp Pro Leu Gly Cys Arg Cys Pro Gln Val Glu 145 150 155 160 Glu Ala Val Ile Gln Ser Gly Cys Lys Leu Val Leu Val Leu Asn 165 170 175 Lys Ser Asp Leu Val Pro Lys Glu Asn Leu Glu Asn Trp Leu Thr Tyr 180 185 190 Leu Asn Lys Glu Leu Pro Thr Val Val Phe Lys Ala Ser Thr Asn Leu 195 200 205 Lys Asn Arg Lys Lys Thr Phe Lys Ile Lys Lys Lys Val Val Pro Phe 210 220 Gln Ser Lys Leu Cys Cys Gly Lys Glu Ala Leu Trp Lys Leu Leu Gly 225 230 235 240 Gly Phe Gln Gln Ser Cys Gly Lys Gly Val Gln Val Gly Val Gly 245 250 255 Phe Pro Asn Val Gly Lys Ser Ser Ile Ile Asn Ser Leu Lys Gln Glu 260 265 270 Arg Ile Cys Ser Val Gly Val Ser Met Gly Leu Thr Arg Ser Met Gln 275 280 285 Ile Val Pro Leu Asp Lys Gln Ile Thr Ile Ile Asp Ser Pro Cys Phe 290 295 300 Ile Ile Ser Pro Cys Asn Ser Pro Ala Ala Leu Ala Leu Arg Ser Pro 305 310 315 320 Ala Ser Ile Glu Val Leu Arg Pro Leu Glu Ala Ala Ser Ala Ile Leu 325 330 335 Page 3

Ser Gln Ala Asp Ser Gln Gln Val Val Leu Lys Tyr Thr Val Pro Gly 340 345 350

Tyr Lys Asp Ser Leu Asp Phe Phe Thr Lys Leu Ala Gln Arg Arg Gly 355 360 365

Leu His Gln Lys Gly Gly Ser Pro Asn Val Glu Ser Ala Ala Lys Leu 370 380

Leu Trp Ser Glu Trp Thr Gly Ala Ser Leu Gly Tyr Tyr Cys His Pro 385 390 395 400

Pro Ala Ser Trp Asn His Ser Pro His Phe Asn Glu Asn Ile Thr Ala 405 410 415

Ile Met Lys Arg Gly Phe Asn Leu Glu Glu Leu Glu Lys Asn Asn Ala 420 430

His Ser Ile Gln Val Leu Lys Gly Pro His Leu Thr Asn Lys Ile Leu 435 440 445

Phe Arg Ser Ser Gly Leu Thr Asn Gly Ile Leu Glu Glu Lys Asp Ile 450 455 460

Pro Glu Glu Ser Pro Lys Gln Thr Glu Asp Gln Gln Asp Gly Asp Asp 465 470 475 480

Gln Glu His Val Thr Gly Glu Lys Asn Ala Glu Ile Ser Asp Val Thr 485 490 495

Pro Val Glu Glu Thr Arg Glu Met Ser Pro Gly Gln Ser Thr Ala Ser 500 505 510

Lys Pro Ser Asp Arg Ser Phe Ile Leu Asp Lys Met Ser Glu Glu Asp 515 520 525

Asp Ala Tyr Asp Phe Thr Thr Asp Tyr Ile 530 535

<210> 3 <211> 1770

<212> DNA

<213> Mus musculus

<400> 3

gaattcggca cgagggttga accgcagttc cagttcgcac gtggcgcccg agaagtcgtg
gtgatcccga gacctcctct gctcctgaag cgtccgcggc caggatgaag aggcctaagt
Page 4

taaagaaagc	gagtaaacgt	atgacctgcc	ataagcgata	taaaattcaa	aaaaaggtcc	180
gagaacatca	tcgaaaatta	aggaaggaag	ctaaaaaacg	gggtcacaag	aagcctagga	240
aggacccagg	tgttccaaat	agtgctccct	ttaaagaggc	tcttcttcgt	gaagctgaac	300
taaggaaaca	gcagcttgaa	gaactaaaac	agcagcagaa	acttgatagg	caaaaagagc	360
aagaaaggaa	aagaaaactt	gaagttagcc	ctggtgatga	gcagtctaat	gtggaaacta	420
gggaggaatc	tgacgagccc	aaaagaaaga	aagccaaagc	aggcaaacag	aatccaaaga	480
agttacattg	ccaggaactt	aaaaaggtga	ttgaagcctc	agacattgtg	ttagaagttt	540
tggatgccag	agatcctctt	ggttgcaggt	gtcctcagat	agaagaagct	gttatccaga	600
gtgggagtaa	gaagctgata	cttgtattaa	ataagtctga	tctagtacca	aaggagaatt	660
tggagaactg	gctaaattat	ttgaataaag	aattgccaac	cgtggtgttc	aaagcctcaa	720
caaacttaaa	gaacagaaag	acattcaaga	taaaaaagaa	gaaagttgtt	ccattccaaa	780
gcaaaatctg	ctgtggcaag	gaagcccttt	ggaagcttct	tggagatttt	cagcagtcct	840
gtggaaagga	tattcaagtt	ggagtgattg	gtttcccaaa	tgtggggaaa	agcagtgtca	900
ttaatagctt	aaaacaagaa	tggatttgca	atgttgggat	ttccatggga	cttacaagga	960
gcatgcagat	tgtcccttta	gacaagcaga	tcacaatcat	agacagtcca	tgcctaatta	1020
tctcaccttg	taactccccc	actgcacttg	cccttcggag	tccagcaagc	attgaggaac	1080
taagaccgct	ggaggctgcc	agtgccattc	tgtctcaggc	tgataatgaa	caggtggtgt	1140
taaaatatac	tgtccctgag	tataaggatt	ctctgcattt	ttttactaaa	cttgctcaaa	1200
gaagaggtct	gcaccaaaaa	ggtggaagcc	caaatgtgga	aagtgctgct	aagctggtgt	1260
ggtctgagtg	gacaggtgcc	tcattaggtt	actattgcca	tcccctgca	tcctggaatc	1320
attctctgca	ttttaatgag	aatattgcag	cagtcatgaa	gaagggcttt	aatctagaag	1380
aactagaaaa	gaataatgca	cacagcatac	aagtcctcaa	gggccctcat	ttaactaata	1440
gaatcctttt	tcggtcttcg	ggcctgacaa	atggaatact	agacgagaag	gacatagtcg	1500
aagagaccag	ggagctgtca	cctgagcaat	caacagcagg	taagccatct	gacgggtcgt	1560
ctgccttgga	tagagcgagt	caagaggatg	aaacctatga	cttcaccaca	gattatatat	1620
aaccgccaca	cactaacgtg	ctctctgtac	gctgtgtagt	ttagtgtatg	atataaactg	1680
tacatcttgt	aaatatgtat	catgttataa	attcaaaata	aaatacaagt	atttgcttgc	1740
aaaaaaaaa	aaaaaaaact	cgactctaga				1770

<sup>&</sup>lt;210> 4 <211> 538 <212> PRT <213> Mus musculus

<400> 4

Met Lys Arg Pro Lys Leu Lys Lys Ala Ser Lys Arg Met Thr Cys His 10 15 Lys Arg Tyr Lys Ile Gln Lys Lys Val Arg Glu His His Arg Lys Leu 20 25 30 Arg Lys Glu Ala Lys Lys Arg Gly His Lys Lys Pro Arg Lys Asp Pro
35 40 45 Gly Val Pro Asn Ser Ala Pro Phe Lys Glu Ala Leu Leu Arg Glu Ala 50 60 Glu Leu Arg Lys Gln Gln Leu Glu Glu Leu Lys Gln Gln Gln Lys Leu 65 70 75 80 Asp Arg Gln Lys Glu Gln Glu Arg Lys Arg Lys Leu Glu Val Ser Pro 85 90 95 Gly Asp Glu Gln Ser Asn Val Glu Thr Arg Glu Glu Ser Asp Glu Pro 100 105 110 Lys Arg Lys Lys Ala Lys Ala Gly Lys Gln Asn Pro Lys Lys Leu His 115 120 125 Cys Gln Glu Leu Lys Lys Val Ile Glu Ala Ser Asp Ile Val Leu Glu 130 135 140 Val Leu Asp Ala Arg Asp Pro Leu Gly Cys Arg Cys Pro Gln Ile Glu 145 150 155 160 Glu Ala Val Ile Gln Ser Gly Ser Lys Leu Ile Leu Val Leu Asn 165 170 175 Lys Ser Asp Leu Val Pro Lys Glu Asn Leu Glu Asn Trp Leu Asn Tyr 180 185 190 Leu Asn Lys Glu Leu Pro Thr Val Val Phe Lys Ala Ser Thr Asn Leu 195 200 205 Lys Asn Arg Lys Thr Phe Lys Ile Lys Lys Lys Lys Val Val Pro Phe 210 215 220 Gln Ser Lys Ile Cys Cys Gly Lys Glu Ala Leu Trp Lys Leu Leu Gly 225 230 235 240 Asp Phe Gln Gln Ser Cys Gly Lys Asp Ile Gln Val Gly Val Ile Gly Page 6

Phe Pro Asn Val Gly Lys Ser Ser Val Ile Asn Ser Leu Lys Gln Glu 260 265 270 Trp Ile Cys Asn Val Gly Ile Ser Met Gly Leu Thr Arg Ser Met Gln 275 280 285 Ile Val Pro Leu Asp Lys Gln Ile Thr Ile Ile Asp Ser Pro Cys Leu 290 295 300 Ile Ile Ser Pro Cys Asn Ser Pro Thr Ala Leu Ala Leu Arg Ser Pro 305 310 315 320 Ala Ser Ile Glu Glu Leu Arg Pro Leu Glu Ala Ala Ser Ala Ile Leu 325 330 335 Ser Gln Ala Asp Asn Glu Gln Val Val Leu Lys Tyr Thr Val Pro Glu 340 345 350 Tyr Lys Asp Ser Leu His Phe Phe Thr Lys Leu Ala Gln Arg Arg Gly 355 360 365 Leu His Gln Lys Gly Gly Ser Pro Asn Val Glu Ser Ala Ala Lys Leu 370 380 Val Trp Ser Glu Trp Thr Gly Ala Ser Leu Gly Tyr Tyr Cys His Pro 385 390 395 400 Pro Ala Ser Trp Asn His Ser Leu His Phe Asn Glu Asn Ile Ala Ala 405 410 415 Val Met Lys Lys Gly Phe Asn Leu Glu Glu Leu Glu Lys Asn Asn Ala 420 425 430 His Ser Ile Gln Val Leu Lys Gly Pro His Leu Thr Asn Arg Ile Leu 435 440 445 Phe Arg Ser Ser Gly Leu Thr Asn Gly Ile Leu Asp Glu Lys Asp Ile 450 455 460 Val Glu Glu Ser Pro Ser Gln Thr Glu Asp Gln Gln Asp Ala Asp Asp 465 470 475 480 Gln Glu Asn Gly Ser Gly Glu Arg Asn Ala Glu Ile Ser Asp Val Ala 485 490 495 Sequence Listing
Pro Val Glu Glu Thr Arg Glu Leu Ser Pro Glu Gln Ser Thr Ala Gly
500 505 510

Lys Pro Ser Asp Gly Ser Ser Ala Leu Asp Arg Ala Ser Gln Glu Asp 515 520 525

Glu Thr Tyr Asp Phe Thr Thr Asp Tyr Ile 530 535

<210> 5

<211> 27

<212> PRT

<213> Homo sapiens

<400> 5

Leu Arg Glu Ala Glu Leu Arg Lys Gln Arg Leu Glu Glu Leu Lys Gln 1 5 10 15

Gln Gln Lys Leu Asp Arg Gln Lys Glu Leu Glu 20 25

<210> 6

<211> 549 <212> PRT

<212> PRT <213> Homo sapiens

<400> 6

Met Lys Arg Pro Lys Leu Lys Lys Ala Ser Lys Arg Met Thr Cys His 1 10 15

Lys Arg Tyr Lys Ile Gln Lys Lys Val Arg Glu His His Arg Lys Leu  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Arg Lys Glu Ala Lys Lys Gln Gly His Lys Lys Pro Arg Lys Asp Pro 35 40 45

Gly Val Pro Asn Ser Ala Pro Phe Lys Glu Ala Leu Leu Arg Glu Ala 50 55 60

Glu Leu Arg Lys Gln Arg Leu Glu Glu Leu Lys Gln Gln Gln Lys Leu 65 70 75 80

Asp Arg Gln Lys Glu Leu Glu Lys Lys Arg Lys Leu Glu Thr Asn Pro 85 90 95

Asp Ile Lys Pro Ser Asn Val Glu Pro Met Glu Lys Glu Phe Gly Leu 100 105 110

Cys Lys Thr Glu Asn Lys Ala Lys Ser Gly Lys Gln Asn Ser Lys Lys Page 8 Leu Tyr Cys Gln Glu Leu Lys Lys Val Ile Glu Ala Ser Asp Val Val 130 135 140 Leu Glu Val Leu Asp Ala Arg Asp Pro Leu Gly Cys Arg Cys Pro Gln 145 150 155 160 Val Glu Glu Ala Ile Val Gln Ser Gly Gln Lys Lys Leu Val Leu Ile 165 170 175 Leu Asn Lys Ser Asp Leu Val Pro Lys Glu Asn Leu Glu Ser Trp Leu 180 185 190 Asn Tyr Leu Lys Lys Glu Leu Pro Thr Val Val Phe Arg Ala Ser Thr 195 200 205 Pro Lys Asp Lys Gly Lys Ile Thr Lys Arg Val Lys Ala Lys Lys 210 220 Asn Ala Ala Pro Phe Arg Ser Glu Val Cys Phe Gly Lys Glu Gly Leu 225 230 235 240 Trp Lys Leu Leu Gly Gly Phe Gln Glu Thr Cys Ser Lys Ala Ile Arg 245 250 255 Val Gly Val Ile Gly Phe Pro Asn Val Gly Lys Ser Ser Ile Ile Asn 260 265 270 Ser Leu Lys Gln Glu Gln Met Cys Asn Val Gly Val Ser Met Gly Leu 275 280 285 Thr Arg Ser Met Gln Val Val Pro Leu Asp Lys Gln Ile Thr Ile Ile 290 295 300 Asp Ser Pro Ser Phe Ile Val Ser Pro Leu Asn Ser Ser Ser Ala Leu 305 310 315 320 Ala Leu Arg Ser Pro Ala Ser Ile Glu Val Val Lys Pro Met Glu Ala Ala Ser Ala Ile Leu Ser Gln Ala Asp Ala Arg Gln Val Val Leu Lys 340 345 350 Tyr Thr Val Pro Gly Tyr Arg Asn Ser Leu Glu Phe Phe Thr Met Leu 355 360 365

120

```
Sequence Listing
Ala Gln Arg Arg Gly Met His Gln Lys Gly Gly Ile Pro Asn Val Glu
370 375 380
Gly Ala Ala Lys Leu Leu Trp Ser Glu Trp Thr Gly Ala Ser Leu Ala
385 390 395
Tyr Tyr Cys His Pro Pro Thr Ser Trp Thr Pro Pro Pro Tyr Phe Asn
Glu Ser Ile Val Val Asp Met Lys Ser Gly Phe Asn Leu Glu Glu Leu
             420
Glu Lys Asn Asn Ala Gln Ser Ile Arg Ala Ile Lys Gly Pro His Leu
435 440 445
Ala Asn Ser Ile Leu Phe Gln Ser Ser Gly Leu Thr Asn Gly Ile Ile
Glu Glu Lys Asp Ile His Glu Glu Leu Pro Lys Arg Lys Glu Arg Lys
465 470 475 480
Gln Glu Glu Arg Glu Asp Asp Lys Asp Ser Asp Gln Glu Thr Val Asp
Glu Glu Val Asp Glu Asn Ser Ser Gly Met Phe Ala Ala Glu Glu Thr
500 505 510
Gly Glu Ala Leu Ser Glu Glu Thr Thr Ala Gly Glu Gln Ser Thr Arg
Ser Phe Ile Leu Asp Lys Ile Ile Glu Glu Asp Asp Ala Tyr Asp Phe 530 540
Ser Thr Asp Tyr Val
<210>
       23
<211>
<212>
<213>
        Artificial Sequence
<220>
<223>
       NS-specific siRNA
```

<220> <221>

<222>

<223>

<400>

misc\_feature

(22)..(23)

n is t

7

Page 10

```
Sequence Listing
                                                                           23
aagaacuaaa acagcagcag ann
<210>
       8
       23
<211>
<212>
      RNA
<213> Artificial Sequence
<220>
<223> Control siRNA for rat cells
<220>
<221>
      misc_feature
<222>
       (22)..(23)
<223> n is t
<400> 8
                                                                           23
aacauucaga cugggaaaug gnn
<210>
<211>
       23
<212>
       RNA
<213>
      Artificial Sequence
<220>
<223> Control siRNA for human cells
<220>
<221>
       misc_feature
<222> (22)...
<223> n is t
       (22)..(23)
<400>
                                                                           23
aaucagacgu ggaccagaag ann
<210> 10
<211>
      549
<212> PRT
<213> Artificial Sequence
<220>
<223> Amino acid sequence of a consensus nucleostemin
<220>
<221> MISC_FEATURE
<222>
       (39)..(39)
<223> Xaa is Arg or Gln
<220>
<221>
<222>
<223>
       MISC_FEATURE
       (45)..(45)
       Xaa is Lys or Arg
<220>
<221>
       MISC_FEATURE
<222> (70)..(70)
<223> Xaa is Gln or Arg
```

III . . . .

Page 11

```
<220>
       MISC_FEATURE
<221>
<222>
<223>
       (86) \dots (86)
       Xaa is Gln or Leu
<220>
<221>
       misc_feature
<222>
       (88)..(88)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
<222>
       misc_feature
       (94)..(95)
<223>
       Xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (97)..(100)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
<222>
       misc_feature (105)..(106)
<223>
       xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (108)..(110)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       MISC_FEATURE
<222>
       (111)..(112)
       xaa can be any naturally occurring amino acid or no amino acid
<223>
<220>
<221>
<222>
<223>
       misc_feature (113)..(117)
       xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (121)..(121)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
<222>
       misc_feature
       (126)..(126)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (130)..(130)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
        (143)..(143)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature (161)..(161)
<222>
```

Page 12

```
Sequence Listing
<223> Xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (165)..(166)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (170)..(170)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (174)..(174)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (176)..(176)
<223>
       xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (190)..(190)
<223>
       xaa can be any naturally occurring amino acid
<220>
<221>
<222>
       misc_feature
       (193)..(193)
<223>
       xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (196)..(196)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (205)..(205)
<223>
       xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (209)..(210)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       MISC_FEATURE
<222>
       (212)..(212)
       xaa can be any naturally occurring amino acid or no amino acid
<223>
<220>
<221>
<222>
       misc_feature
       (213)..(214)
<223>
       xaa can be any naturally occurring amino acid
<220>
       MISC_FEATURE
<221>
<222>
       (216)..(216)
      xaa can be any naturally occurring amino acid or no amino acid
<223>
<220>
```

Page 13

#### Sequence Listing <221> misc\_feature <222> (218)..(220)<223> Xaa can be any naturally occurring amino acid <220> <221> <222> misc\_feature (222)..(222) Xaa can be any naturally occurring amino acid <223> <220> <221> MISC\_FEATURE (224)..(225) <222> Xaa can be any naturally occurring amino acid or no amino acid <223> <220> <221> misc\_feature <222> (226)..(227)Xaa can be any naturally occurring amino acid <223> <220> <221> <222> <223> misc\_feature (230)..(230)xaa can be any naturally occurring amino acid <220> misc\_feature <221> <222> (232)..(233)Xaa can be any naturally occurring amino acid <223> <220> <221> <222> misc\_feature (235)..(235) Xaa can be any naturally occurring amino acid <223> <220> <221> misc\_feature <222> (239)..(239)xaa can be any naturally occurring amino acid <223> <220> <221> misc\_feature <222> (246)..(246)<223> Xaa can be any naturally occurring amino acid <220> <221> <222> misc\_feature (249)..(250)Xaa can be any naturally occurring amino acid <223> <220> misc\_feature <221> <222> (252)..(252)Xaa can be any naturally occurring amino acid <223>

Xaa can be any naturally occurring amino acid

<220> <221> <222>

<223>

<220>

misc\_feature (254)..(256)

```
<220>
<221>
<222>
       misc_feature
       (270)..(270)
<223>
       Xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (278)..(279)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
<222>
       misc_feature (281)..(281)
<223>
       Xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
       (284)..(284)
<222>
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
<222>
       misc_feature
       (294)..(294)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
       (308)..(309)
<222>
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (311)..(311)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
<222>
       misc_feature
       (314)..(314)
       xaa can be any naturally occurring amino acid
<223>
<220>
       misc_feature
<221>
<222>
       (317)..(318)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (330)..(332)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (334)..(334)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
<222>
       misc_feature
       (346)..(347)
       Xaa can be any naturally occurring amino acid
<223>
<220>
       misc_feature
<221>
```

#### Sequence Listing <222> (357)..(357)Xaa can be any naturally occurring amino acid <223> <220> <221> <222> misc\_feature (359)..(360) <223> Xaa can be any naturally occurring amino acid <220> <221> misc\_feature <222> (363)..(363) Xaa can be any naturally occurring amino acid <223> <220> <221> misc\_feature <222> (367)..(367)xaa can be any naturally occurring amino acid <223> <220> misc\_feature <221> <222> <223> (374)..(374)Xaa can be any naturally occurring amino acid <220> <221> <222> misc\_feature (380)..(380)<223> Xaa can be any naturally occurring amino acid <220> <221> misc\_feature <222> (385)..(385)<223> Xaa can be any naturally occurring amino acid <220> <221> misc\_feature <222> (390)..(390)Xaa can be any naturally occurring amino acid <223> <220> <221> misc\_feature <222> (400)..(400)<223> xaa can be any naturally occurring amino acid <220> <221> misc\_feature <222> <223> (407)..(407)Xaa can be any naturally occurring amino acid <220> misc\_feature <221> <222> (410)..(414)<223> Xaa can be any naturally occurring amino acid <220> misc\_feature <221> <222> (418)..(418) <223> Xaa can be any naturally occurring amino acid <220> <221> misc\_feature (420)..(422) <222> <223> xaa can be any naturally occurring amino acid

```
<220>
<221>
<222>
       misc_feature
       (425)..(425)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (438)..(438)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
<222>
       misc_feature (441)..(443)
<223>
       Xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (449)..(449)
       xaa can be any naturally occurring amino acid
<223>
<220>
       misc_feature (451)..(451)
<221>
<222>
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (455)..(455)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (464)..(465)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
<222>
       misc_feature (470)..(470)
<223>
       Xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (473)..(473)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (475)..(477)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
<223>
       (479)..(480)
       xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (482)..(483)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       MISC_FEATURE
       (484)..(489)
<222>
```

```
Sequence Listing
<223> Xaa can be any naturally occurring amino acid or no amino acid
<220>
<221>
<222>
       misc_feature
       (490)..(490)
       Xaa can be any naturally occurring amino acid
<223>
<220>
       misc_feature
<221>
<222>
       (494)..(497)
       Xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (499)..(503)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (505)..(509)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (513)..(513)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
<222>
       misc_feature
       (515)..(520)
       xaa can be any naturally occurring amino acid
<223>
<220>
       misc_feature
<221>
<222>
       (523)..(525)
<223>
       Xaa can be any naturally occurring amino acid
<220>
       misc_feature (527)..(528)
<221>
<222>
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
       misc_feature
<222>
       (530)..(531)
       xaa can be any naturally occurring amino acid
<223>
<220>
<221>
       misc_feature
<222>
       (534)..(537)
<223>
       Xaa can be any naturally occurring amino acid
<220>
<221>
<222>
       misc_feature (540)..(541)
<223>
       Xaa can be any naturally occurring amino acid
<220>
       misc_feature
<221>
<222>
       (545)..(545)
       Xaa can be any naturally occurring amino acid
<223>
<220>
```

Page 18

<221> misc\_feature

<222> (549)..(549)

<223> Xaa can be any naturally occurring amino acid

<400> 10

Met Lys Arg Pro Lys Leu Lys Lys Ala Ser Lys Arg Met Thr Cys His 1 10 15

Lys Arg Tyr Lys Ile Gln Lys Lys Val Arg Glu His His Arg Lys Leu 20 25 30

Arg Lys Glu Ala Lys Lys Xaa Gly His Lys Lys Pro Xaa Lys Asp Pro
35 40 45

Gly Val Pro Asn Ser Ala Pro Phe Lys Glu Ala Leu Leu Arg Glu Ala 50 55 60

Glu Leu Arg Lys Gln Xaa Leu Glu Glu Leu Lys Gln Gln Gln Lys Leu 65 70 75 80

Asp Arg Gln Lys Glu Xaa Glu Xaa Lys Arg Lys Leu Glu Xaa Xaa Pro 85 90 95

Xaa Xaa Xaa Ser Asn Val Glu Xaa Xaa Glu Xaa Xaa Xaa Xaa Xaa 100 105 110

Xaa Xaa Xaa Xaa Lys Ala Lys Xaa Gly Lys Gln Asn Xaa Lys Lys 115 120 125

Leu Xaa Cys Gln Glu Leu Lys Lys Val Ile Glu Ala Ser Asp Xaa Val 130 135 140

Leu Glu Val Leu Asp Ala Arg Asp Pro Leu Gly Cys Arg Cys Pro Gln 145 150 155 160

Xaa Glu Glu Ala Xaa Xaa Gln Ser Gly Xaa Lys Lys Leu Xaa Leu Xaa 165 170 175

Leu Asn Lys Ser Asp Leu Val Pro Lys Glu Asn Leu Glu Xaa Trp Leu 180 185 190

Xaa Tyr Leu Xaa Lys Glu Leu Pro Thr Val Val Phe Xaa Ala Ser Thr 195 200 205

Xaa Xaa Lys Xaa Xaa Lys Xaa Thr Xaa Xaa Lys Xaa Lys Xaa 210 215 220

Xaa Xaa Xaa Pro Phe Xaa Ser Xaa Xaa Cys Xaa Gly Lys Glu Xaa Leu Page 19

Trp Lys Leu Leu Gly Xaa Phe Gln Xaa Xaa Cys Xaa Lys Xaa Xaa Xaa 245 250 255 Val Gly Val Xaa Gly Phe Pro Asn Val Gly Lys Ser Ser Xaa Ile Asn 260 265 270 Ser Leu Lys Gln Glu Xaa Xaa Cys Xaa Val Gly Xaa Ser Met Gly Leu 275 280 285 Thr Arg Ser Met Gln Xaa Val Pro Leu Asp Lys Gln Ile Thr Ile Ile 290 295 300 Asp Ser Pro Xaa Xaa Ile Xaa Ser Pro Xaa Asn Ser Xaa Xaa Ala Leu Ala Leu Arg Ser Pro Ala Ser Ile Glu Xaa Xaa Xaa Pro Xaa Glu Ala Ala Ser Ala Ile Leu Ser Gln Ala Asp. Xaa Xaa Gln Val Val Leu Lys 340 345 350 Tyr Thr Val Pro Xaa Tyr Xaa Xaa Ser Leu Xaa Phe Phe Thr Xaa Leu 355 360 Ala Gln Arg Arg Gly Xaa His Gln Lys Gly Gly Xaa Pro Asn Val Glu 370 380 Xaa Ala Ala Lys Leu Xaa Trp Ser Glu Trp Thr Gly Ala Ser Leu Xaa 385 390 395 400 Tyr Tyr Cys His Pro Pro Xaa Ser Trp Xaa Xaa Xaa Xaa Xaa Phe Asn Glu Xaa Ile Xaa Xaa Xaa Met Lys Xaa Gly Phe Asn Leu Glu Glu Leu 420 Glu Lys Asn Asn Ala Xaa Ser Ile Xaa Xaa Xaa Lys Gly Pro His Leu 435 440 445 Xaa Asn Xaa Ile Leu Phe Xaa Ser Ser Gly Leu Thr Asn Gly Ile Xaa

Xaa Glu Lys Asp Ile Xaa Glu Glu Xaa Pro Xaa Xaa Xaa Glu Xaa Xaa

### Sequence Listing Gln Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asp Gln Glu Xaa Xaa Xaa 490 Xaa Glu Xaa Xaa Xaa Xaa Ser Xaa Xaa Xaa Xaa Glu Glu Thr 500 505 Xaa Glu Xaa Xaa Xaa Xaa Xaa Thr Ala Xaa Xaa Xaa Ser Xaa Xaa 520 Ser Xaa Xaa Leu Asp Xaa Xaa Xaa Glu Asp Xaa Xaa Tyr Asp Phe 530 535 Xaa Thr Asp Tyr Xaa 545 <210> 11 1926 <211> <212> DNA <213> Artificial Sequence <220> <223> NS2 <220> <221> CDS <222> (122)..(1852)<400> gctgcgcact cctggactgg cgacgttgtg cttctaacag ctctccgagg tccctgccgg 60 120 aagtgtagga agaagcagac agatttgaac atctctgttt ccagcttctc tgatcatcat g atg aag att aga cac aaa aac aaa aaa cca ggt aaa ggt tcc aaa ggc Met Lys Ile Arg His Lys Asn Lys Lys Pro Gly Lys Gly Ser Lys Gly 1 5 10 15 169 217 tgt aag aag cct gca agg caa aat ggg aag aaa gta acc tcc aga cca Cys Lys Lys Pro Ala Arg Gln Asn Gly Lys Lys Val Thr Ser Arg Pro tca tct gct ccc cag att gtt cat ggc aat gac cat gcc agt cgc gag Ser Ser Ala Pro Gln Ile Val His Gly Asn Asp His Ala Ser Arg Glu 265 313 gcc gaa tta aag aag aaa agg gtc gag gag atg agg gag aag cag caa Ala Glu Leu Lys Lys Lys Arg Val Glu Glu Met Arg Glu Lys Gln Gln 50 55 60 gtt gcc cgg gag caa gag aga cag aga cac agg acc atg gag agc tat Val Ala Arg Glu Gln Glu Arg Gln Arg His Arg Thr Met Glu Ser Tyr 65 70 75 80 361 409 tqt caq qat qtc ctq aaa cqt cag cag gaa ttt gaa caa aag gag gaa CЎS GÌN ĂSP Val Leŭ Lys Arg Gìn Gìn Gìu Phe Glu Gìn Lys Gìu Gìu

gtt ttg cag gaa tta aac atg ttt cct cag ttg gat gat gag gcc aca

Page 21

457

۷al	Leu	Gln	Glu 100	Leu	Asn	Met	Phe		equer G1n				Glu 110	Ala	Thr	
agg Arg	aag Lys	gcc Ala 115	tat Tyr	tac Tyr	aag Lys	gaa Glu	ttc Phe 120	cgg Arg	aag Lys	gtg Val	gta Val	gag Glu 125	tac Tyr	tct Ser	gat Asp	505
gtg Val	att Ile 130	ctg Leu	gaa Glu	gtc Val	cta Leu	gat Asp 135	gcc Ala	aga Arg	gac Asp	cca Pro	ttg Leu 140	ggc Gly	tgc Cys	cgc Arg	tgt Cys	553
ttc Phe 145	cag Gln	atg Met	gag Glu	gag Glu	act Thr 150	gtc Val	ctt Leu	cgt Arg	gca Ala	gaa Glu 155	ggc Gly	aac Asn	aag Lys	aag Lys	ctg Leu 160	601
gtc Val	ttg Leu	gtc val	tta Leu	aat Asn 165	aag Lys	ata Ile	gat Asp	ctc Leu	gtt Val 170	ccc Pro	aag Lys	gag Glu	att Ile	gtg Val 175	gaa Glu	649
aag Lys	tgg Trp	ctg Leu	gaa Glu 180	tac Tyr	ctt Leu	ctc Leu	aat Asn	gaa Glu 185	ctg Leu	cca Pro	act Thr	gtg Val	gct Ala 190	ttc Phe	aag Lys	697
gcc Ala	agc Ser	acc Thr 195	cag Gln	cat His	cat His	cag Gln	gtc Val 200	aaa Lys	aac Asn	ttg Leu	act Thr	cgt Arg 205	tgt Cys	aaa Lys	gtt Val	745
cca Pro	gtg Val 210	gac Asp	cag Gln	gcc Ala	tct Ser	gag Glu 215	tcg Ser	ctt Leu	ttg Leu	aaa Lys	agc Ser 220	aga Arg	gcc Ala	tgc Cys	ttt Phe	793
gga Gly 225	gcc Ala	gaa Glu	aat Asn	ctc Leu	atg Met 230	agg Arg	gtc Val	ctg Leu	ggg Gly	aac Asn 235	tat Tyr	tgt Cys	cgc Arg	ctg Leu	ggg G1y 240	841
gaa Glu	gtg Val	cgt Arg	ggc Gly	cac His 245	att Ile	cgt Arg	gtg Val	ggt Gly	gtt Val 250	gta Val	ggc Gly	ctt Leu	ccc Pro	aat Asn 255	gtg Val	889
ggg Gly	aag Lys	agc Ser	agt Ser 260	ctg Leu	atc Ile	aat Asn	agc Ser	ctg Leu 265	aag Lys	cgc Arg	agc Ser	cgt Arg	gct Ala 270	tgt Cys	agt Ser	937
gtg Val	gga Gly	gct Ala 275	gtt Val	cct Pro	ggt Gly	gtc Val	aca Thr 280	aaa Lys	ttc Phe	atg Met	cag Gln	gag Glu 285	gtc Val	tac Tyr	cta Leu	985
gac Asp	aag Lys 290	ttt Phe	atc Ile	agg Arg	ctt Leu	ctg Leu 295	gat Asp	gca Ala	cca Pro	ggc Gly	att Ile 300	gtc Val	cca Pro	gga Gly	ccc Pro	1033
aat Asn 305	tca Ser	gag Glu	gtg Val	ggc Gly	acc Thr 310	atc Ile	ctg Leu	cgt Arg	aat Asn	tgc Cys 315	atc Ile	cat His	gtg Val	cag Gln	aag Lys 320	1081
ctg Leu	gca Ala	gac Asp	cct Pro	gtg Val 325	acc Thr	ccg Pro	gtg Val	gag Glu	acc Thr 330	atc Ile	ctt Leu	cag Gln	cgc Arg	tgc Cys 335	aac Asn	1129
ctg Leu	gag Glu	gag Glu	att Ile 340	tcc Ser	agc Ser	tac Tyr	tat Tyr	ggt Gly 345	gta Val	tct Ser	gga Gly	ttc Phe	cag Gln 350	acg Thr	act Thr	1177

						equer							
gag cac t Glu His I	ttt ctg Phe Leu 355	act go Thr Al	a gtg a Val	gcc Ala 360	cat His	cgc Arg	ttg Leu	gga Gly	aag Lys 365	aag Lys	aag Lys	aag Lys	1225
gga ggt g Gly Gly v 370	gta tat Val Tyr	agt ca Ser Gl	g gaa n Glu 375	cag Gln	gct Ala	gcc Ala	aaa Lys	gct Ala 380	gtg Val	ctg Leu	gct Ala	gac Asp	1273
tgg gtg a Trp Val S 385			e Ser										1321
act ctg ( Thr Leu I	ccc acc Pro Thr	cat ct His Le 405	c agt u Ser	gct Ala	gag Glu	att Ile 410	gtt Val	aag Lys	gag Glu	atg Met	act Thr 415	gag Glu	1369
gtc ttt ( Val Phe /													1417
tgc tta ( Cys Leu /	gct gtg Ala Val 435	gga ga Gly Gl	a tcc u Ser	gat Asp 440	gag Glu	ctg Leu	ttg Leu	ggt Gly	gac Asp 445	atg Met	gac Asp	cca Pro	1465
caa gaa a Gln Glu M 450	atg gag Met Glu	gtc ag Val Ar	g tgg g Trp 455	ctc Leu	cat His	tct Ser	cca Pro	ctg Leu 460	gtg val	aaa Lys	ata Ile	gca Ala	1513
gat gct a Asp Ala : 465	att gaa Ile Glu	aat ag Asn Ar 47	g Ser	acc Thr	gtg Val	tat Tyr	aag Lys 475	att Ile	gga Gly	aat Asn	ctc Leu	act Thr 480	1561
ggg tat i Gly Tyr (	tgt acc Cys Thr	aaa cc Lys Pr 485	a aac o Asn	cgt Arg	aat Asn	cag Gln 490	atg Met	ggg Gly	tgg Trp	cct Pro	aaa Lys 495	cgc Arg	1609
aat gtg ( Asn Val													1657
tct gtg ( Ser Val /	gac cgc Asp Arg 515	cgc cc Arg Pr	g atg o Met	ttg Leu 520	cag Gln	agg Arg	atc Ile	ctg Leu	gag Glu 525	aca Thr	gac Asp	cca Pro	1705
ctt cag Leu Gln ( 530	caa ggc Gln Gly	cag go Gln Al	t ctg a Leu 535	gaa Glu	tct Ser	gcc Ala	ttg Leu	aag Lys 540	aat Asn	aag Lys	aaa Lys	aaa Lys	1753
ttg cag a Leu Gln i 545	aag cgt Lys Arg	tca ga Ser As 55	p Lys	atc Ile	gcc Ala	act Thr	aag Lys 555	ttg Leu	tct Ser	gac Asp	tcc Ser	atg Met 560	1801
atg tcc a Met Ser M													1849
tga gcag	ctgacc 1	ttcccc	tca t	actg	caag	t act	tgcti	tccc	gtg	gat	999		1902
agagtcag	at gcct	ttcatt	ctct										1926

<212> PRT

<213> Artificial Sequence

<220>

<223> NS2

<400> 12

Met Lys Ile Arg His Lys Asn Lys Lys Pro Gly Lys Gly Ser Lys Gly 10 15

Cys Lys Lys Pro Ala Arg Gln Asn Gly Lys Lys Val Thr Ser Arg Pro
20 25 30

Ser Ser Ala Pro Gln Ile Val His Gly Asn Asp His Ala Ser Arg Glu 35 40 45

Ala Glu Leu Lys Lys Lys Arg Val Glu Glu Met Arg Glu Lys Gln Gln 50 60

Val Ala Arg Glu Gln Glu Arg Gln Arg His Arg Thr Met Glu Ser Tyr 65 70 75 80

Cys Gln Asp Val Leu Lys Arg Gln Gln Glu Phe Glu Gln Lys Glu Glu 85 90 95

Val Leu Gln Glu Leu Asn Met Phe Pro Gln Leu Asp Asp Glu Ala Thr 100 105 110

Arg Lys Ala Tyr Tyr Lys Glu Phe Arg Lys Val Val Glu Tyr Ser Asp 115 120 125

Val Ile Leu Glu Val Leu Asp Ala Arg Asp Pro Leu Gly Cys Arg Cys 130 140

Phe Gln Met Glu Glu Thr Val Leu Arg Ala Glu Gly Asn Lys Leu 145 150 155 160

Val Leu Val Leu Asn Lys Ile Asp Leu Val Pro Lys Glu Ile Val Glu 165 170 175

Lys Trp Leu Glu Tyr Leu Leu Asn Glu Leu Pro Thr Val Ala Phe Lys 180 185 190

Ala Ser Thr Gln His His Gln Val Lys Asn Leu Thr Arg Cys Lys Val 195 200 205

Pro Val Asp Gln Ala Ser Glu Ser Leu Leu Lys Ser Arg Ala Cys Phe 210 220

Gly Ala Glu Asn Leu Met Arg Val Leu Gly Asn Tyr Cys Arg Leu Gly 225 230 235 240 Glu Val Arg Gly His Ile Arg Val Gly Val Gly Leu Pro Asn Val 245 250 255 Gly Lys Ser Ser Leu Ile Asn Ser Leu Lys Arg Ser Arg Ala Cys Ser 260 265 270 Val Gly Ala Val Pro Gly Val Thr Lys Phe Met Gln Glu Val Tyr Leu 275 280 285 Asp Lys Phe Ile Arg Leu Leu Asp Ala Pro Gly Ile Val Pro Gly Pro 290 295 300 Asn Ser Glu Val Gly Thr Ile Leu Arg Asn Cys Ile His Val Gln Lys 305 310 315 320 Leu Ala Asp Pro Val Thr Pro Val Glu Thr Ile Leu Gln Arg Cys Asn 325 330 335 Leu Glu Glu Ile Ser Ser Tyr Tyr Gly Val Ser Gly Phe Gln Thr Thr 340 345 350 Glu His Phe Leu Thr Ala Val Ala His Arg Leu Gly Lys Lys Lys Lys 365 Gly Gly Val Tyr Ser Gln Glu Gln Ala Ala Lys Ala Val Leu Ala Asp 370 375 380 Trp Val Ser Gly Lys Ile Ser Phe Tyr Thr Leu Pro Pro Pro Thr His 385 390 395 400 Thr Leu Pro Thr His Leu Ser Ala Glu Ile Val Lys Glu Met Thr Glu Val Phe Asp Ile Glu Asp Thr Glu His Ala Asn Glu Asp Thr Met Glu
420 425 430 Cys Leu Ala Val Gly Glu Ser Asp Glu Leu Leu Gly Asp Met Asp Pro 435 440 445 Gln Glu Met Glu Val Arg Trp Leu His Ser Pro Leu Val Lys Ile Ala 450 455 460 Asp Ala Ile Glu Asn Arg Ser Thr Val Tyr Lys Ile Gly Asn Leu Thr 465 470 475 480 Page 25

Asn Val Asp His His Cys Pro Gln Asn Asn Arg Val Val Glu Val Ser 500 505 510	
Ser Val Asp Arg Arg Pro Met Leu Gln Arg Ile Leu Glu Thr Asp Pro 515 520 525	
Leu Gln Gln Gly Gln Ala Leu Glu Ser Ala Leu Lys Asn Lys Lys 530 535 540	
Leu Gln Lys Arg Ser Asp Lys Ile Ala Thr Lys Leu Ser Asp Ser Met 545 550 560	
Met Ser Met Leu Asp Leu Ser Gly Asn Ser Asp Asp Cys Ala Gly Asp 565 570	
<210> 13 <211> 2359 <212> DNA <213> Artificial Sequence	
<220> <223> NS3	
<220> <221> CDS <222> (111)(2297)	
<221> CDS	60
<221> CDS <222> (111)(2297) <400> 13	60 116
<221> CDS <222> (111)(2297) <400> 13 gtcgacccac gcgtccgcca acgtgcttca cacaggacgc tttcccggct gggaagtcgt gaagtggttt acctcgcgag tagcagagcg gtgtcggtac tgtcgtcagg atg gtg Met Val	
<pre>&lt;221&gt; CDS &lt;222&gt; (111)(2297)  &lt;400&gt; 13 gtcgacccac gcgtccgcca acgtgcttca cacaggacgc tttcccggct gggaagtcgt gaagtggttt acctcgcgag tagcagagcg gtgtcggtac tgtcgtcagg atg gtg</pre>	116
<pre>&lt;221&gt; CDS &lt;222&gt; (111)(2297)  &lt;400&gt; 13 gtcgacccac gcgtccgcca acgtgcttca cacaggacgc tttcccggct gggaagtcgt gaagtggttt acctcgcgag tagcagagcg gtgtcggtac tgtcgtcagg atg gtg</pre>	116 164
<pre>&lt;221&gt; CDS &lt;222&gt; (111)(2297)  &lt;400&gt; 13 gtcgacccac gcgtccgcca acgtgcttca cacaggacgc tttcccggct gggaagtcgt gaagtggttt acctcgcgag tagcagagcg gtgtcggtac tgtcgtcagg atg gtg Met Val 1  aag ccc aag tac aaa gga cgg agc acc atc aac cgc tcg gcg gcc agc Lys Pro Lys Tyr Lys Gly Arg Ser Thr Ile Asn Arg Ser Ala Ala Ser 5 10 15  acc aac cca gat cga gta cag gga gct ggc ggc caa aac atg agg gat Thr Asn Pro Asp Arg Val Gln Gly Ala Gly Gly Gln Asn Met Arg Asp 20 25 30  cgg ggc aca att cgg cgc ctg aat atg tac agg caa aag gag cgc agg Arg Gly Thr Ile Arg Arg Leu Asn Met Tyr Arg Gln Lys Glu Arg Arg</pre>	116 164 212

Ala	Ser	Gly	Thr 70	۷a٦	Ala	Arg	٧a٦	Se Glu 75	equer Pro	nce l Asn	isti Ile	ing Lys	Trp 80	Phe	Gly	
aat Asn	act Thr	cgt Arg 85	gtg Val	atc Ile	aag Lys	cag Gln	gca Ala 90	tca Ser	tta Leu	caa Gln	aaa Lys	ttt Phe 95	caa Gln	gag Glu	gaa Glu	404
atg Met	gat Asp 100	aaa Lys	gtt Val	atg Met	aag Lys	gat Asp 105	cca Pro	tac Tyr	aaa Lys	gtt val	gtc Val 110	atg Met	aaa Lys	caa Gln	agc Ser	452
aaa Lys 115	tta Leu	ccg Pro	atg Met	tct Ser	ctt Leu 120	ctg Leu	cac His	gat Asp	cga Arg	atc Ile 125	cag Gln	cct Pro	cat His	aac Asn	gca Ala 130	500
aaa Lys	gtc Val	cac His	att Ile	ctt Leu 135	gat Asp	act Thr	gaa Glu	agc Ser	ttt Phe 140	gaa Glu	agt Ser	aca Thr	ttt Phe	ggc Gly 145	cca Pro	548
aag Lys	tca Ser	cag Gln	aga Arg 150	aag Lys	cgg Arg	cca Pro	aac Asn	ttg Leu 155	ttt Phe	gca Ala	agt Ser	gat Asp	atg Met 160	caa Gln	tcc Ser	596
ctt Leu	cta Leu	gaa Glu 165	aac Asn	gct Ala	gaa Glu	atg Met	tct Ser 170	act Thr	gag Glu	agc Ser	tat Tyr	gac Asp 175	cag Gln	ggc Gly	aag Lys	644
gac Asp	cgt Arg 180	gat Asp	ttg Leu	gtg Val	atg Met	gag Glu 185	gac Asp	act Thr	ggt Gly	gta Val	aga Arg 190	aat Asn	gaa Glu	gct Ala	caa Gln	692
gaa Glu 195	gag Glu	ata Ile	tat Tyr	aaa Lys	aaa Lys 200	ggg Gly	cag Gln	tca Ser	aaa Lys	aga Arg 205	ata Ile	tgg Trp	gga Gly	gaa Glu	ctc Leu 210	740
tac Tyr	aag Lys	gtg Val	ata Ile	gac Asp 215	tca Ser	tca Ser	gat Asp	gtt Val	gtc Val 220	gtt Val	caa Gln	gtc Val	ctt Leu	gac Asp 225	gct Ala	788
aga Arg	gat Asp	ccg Pro	atg Met 230	ggc Gly	act Thr	cgt Arg	tcc Ser	ccc Pro 235	cac His	atc Ile	gaa Glu	gct Ala	tac Tyr 240	ttg Leu	aaa Lys	836
aag Lys	gaa Glu	aaa Lys 245	ccc Pro	tgg Trp	aaa Lys	cat His	ctc Leu 250	att Ile	ttt Phe	gta Val	ctc Leu	aat Asn 255	aag Lys	tgt Cys	gac Asp	884
ctt Leu	gtt Val 260	cca Pro	act Thr	tgg Trp	gca Ala	acc Thr 265	aaa Lys	cga Arg	tgg Trp	gtt Val	gct Ala 270	gtg Val	ctc Leu	tcc Ser	cag Gln	932
gac Asp 275	tac Tyr	cca Pro	aca Thr	ctg Leu	gct Ala 280	ttc Phe	cat His	gcg Ala	agc Ser	ctc Leu 285	acc Thr	aat Asn	ccc Pro	ttt Phe	ggg Gly 290	980
aag Lys	gga Gly	gca Ala	ttc Phe	att Ile 295	cag Gln	ctt Leu	ctg Leu	cgg Arg	cag Gln 300	ttt Phe	ggg Gly	aag Lys	ttg Leu	cac His 305	aca Thr	1028
gac Asp	aag Lys	aaa Lys	caa Gln 310	atc Ile	agt Ser	gtt Val	ggg Gly	ttc Phe 315	att Ile	ggc Gly	tat Tyr	cca Pro	aat Asn 320	gta Val	ggc Gly	1076

							tta Leu 330	cga	tcc	aag		gtt				1124
gcc Ala	ccc Pro 340	att Ile	gct Ala	gga Gly	gaa Glu	aca Thr 345	aag Lys	gtc Val	tgg Trp	cag Gln	tat Tyr 350	att Ile	acc Thr	ttg Leu	atg Met	1172
cgt Arg 355	cgt Arg	ata Ile	ttc Phe	ctg Leu	att Ile 360	gac Asp	tgc Cys	cct Pro	ggt Gly	gtg Val 365	gtt Val	tac Tyr	cca Pro	tct Ser	gag Glu 370	1220
							ctc Leu								aaa Lys	1268
							att Ile									1316
cca Pro	gag Glu	tat Tyr 405	atc Ile	agc Ser	aag Lys	acg Thr	tac Tyr 410	aag Lys	att Ile	gag Glu	tcc Ser	tgg Trp 415	gag Glu	aac Asn	gcg Ala	1364
gag Glu	gac Asp 420	ttt Phe	ctt Leu	gag Glu	aag Lys	cta Leu 425	gct Ala	ctc Leu	cgc Arg	act Thr	ggg Gly 430	aag Lys	tta Leu	ctg Leu	aag Lys	1412
ggt Gly 435	gga Gly	gag Glu	cct Pro	gac Asp	atg Met 440	ctg Leu	act Thr	gtg Val	agc Ser	aag Lys 445	atg Met	gtt Val	ctc Leu	aat Asn	gac Asp 450	1460
tgg Trp	cag Gln	aga Arg	ggc Gly	cga Arg 455	atc Ile	cct Pro	ttc Phe	ttt Phe	gtc Val 460	aag Lys	ccg Pro	ccc Pro	aat Asn	gca Ala 465	gag Glu	1508
							cca Pro									1556
aca Thr	gaa Glu	aca Thr 485	acc Thr	cag Gln	aac Asn	aac Asn	cca Pro 490	gaa Glu	gaa Glu	gag Glu	acc Thr	aca Thr 495	gaa Glu	aca Thr	gaa Glu	1604
							act Thr									1652
tct Ser 515	cag Gln	gat Asp	aga Arg	aac Asn	tca Ser 520	gag Glu	atg Met	caa Gln	cag Gln	atc Ile 525	ctc Leu	gca Ala	cga Arg	gtt Val	cgc Arg 530	1700
cag Gln	aac Asn	ttt Phe	ggc Gly	aaa Lys 535	atc Ile	aac Asn	gtg Val	ggg Gly	cct Pro 540	cag Gln	ttt Phe	tct Ser	gcg Ala	gat Asp 545	gac Asp	1748
ctg Leu	gtg Val	cct Pro	gtg Val 550	gag Glu	atg Met	tca Ser	gac Asp	ttg Leu 555	gaa Glu	gat Asp	ctg Leu	gaa Glu	agc Ser 560	tct Ser	ggg Gly	1796
gaa Glu	gag Glu	gaa Glu 565	gaa Glu	cag Gln	gag Glu	cag Gln	gaa Glu 570	cag Gln	Pro	ggg Gly age	Glu	gat Asp 575	gcc Ala	gag Glu	gaa Glu	1844

Page 28

									•							
gag Glu	cgc Arg 580	tcc Ser	cca Pro	gac Asp	act Thr	cag Gln 585	gag Glu	gaa Glu	cca Pro	gtg Val	gga Gly 590	aac Asn	gac Asp	acc Thr	aag Lys	1892
gcc Ala 595	gtg Val	ctc Leu	aga Arg	gcc Ala	ctg Leu 600	gat Asp	gag Glu	aag Lys	att Ile	gcc Ala 605	aag Lys	tac Tyr	cag Gln	agg Arg	ttt Phe 610	1940
cta Leu	aat Asn	aaa Lys	gct Ala	aaa Lys 615	gct Ala	aaa Lys	aag Lys	ttc Phe	tct Ser 620	gcc Ala	gtc Val	aga Arg	ata Ile	tcc Ser 625	aag Lys	1988
gac Asp	tta Leu	agt Ser	gaa Glu 630	aag Lys	gtt Val	ttt Phe	gca Ala	aaa Lys 635	tac Tyr	aaa Lys	gaa Glu	gag Glu	aag Lys 640	aaa Lys	aca Thr	2036
tct Ser	gca Ala	gaa Glu 645	gac Asp	agt Ser	gat Asp	gca Ala	gca Ala 650	ccc Pro	acc Thr	aaa Lys	aag Lys	gca Ala 655	agg Arg	aag Lys	tgg Trp	2084
gat Asp	gca Ala 660	cag Gln	atg Met	gaa Glu	gaa Glu	gaa Glu 665	cct Pro	tca Ser	aat Asn	aag Lys	act Thr 670	cag Gln	agg Arg	atg Met	ctg Leu	2132
acg Thr 675	tgt Cys	aag Lys	gaa Glu	cgg Arg	agg Arg 680	aga Arg	gca Ala	gca Ala	cgg Arg	cag Gln 685	caa Gln	caa Gln	tcc ser	aaa Lys	aaa Lys 690	2180
gtt Val	ggt Gly	gtg val	cgt Arg	tac Tyr 695	tac Tyr	gag Glu	aca Thr	cac His	aat Asn 700	gtg Val	aaa Lys	aac Asn	agg Arg	aac Asn 705	agg Arg	2228
aac Asn	aaa Lys	aag Lys	aag Lys 710	acg Thr	agc Ser	gac Asp	tca Ser	gag Glu 715	gga Gly	cag Gln	aaa Lys	cac His	aga Arg 720	cgc Arg	aac Asn	2276
aag Lys	ttc Phe	aga Arg 725	cag Gln	aag Lys	cag Gln	taa	ctg	cgaga	aaa (	gctg <sup>.</sup>	ttta <sup>.</sup>	tt a	aatt	atac	a	2327
aaaa	ataa	aaa a	aaaa	aaaa	aa a	aggg	cggc	c gc								2359
<210 <210 <210 <210	1> 2>	14 728 PRT Arti	ficia	al S	eque	nce										
<220 <22		NS3														
<40	0> :	14														
Met 1	Val	Lys	Pro	Lys 5	Tyr	Lys	Gly	Arg	Ser 10	Thr	Ile	Asn	Arg	Ser 15	Ala	
Ala	Ser	Thr	Asn 20	Pro	Asp	Arg	۷al	Gln 25	Gly	Ala	Gly	Gly	G]n 30	Asn	Met	

Arg Asp Arg Gly Thr Ile Arg Arg Leu Asn Met Tyr Arg Gln Lys Glu Page 29 Arg Arg Asn Ser Arg Gly Lys Val Ile Lys Pro Leu Gln Tyr Gln Ser 50 60 Thr Val Ala Ser Gly Thr Val Ala Arg Val Glu Pro Asn Ile Lys Trp 65 70 75 80 Phe Gly Asn Thr Arg Val Ile Lys Gln Ala Ser Leu Gln Lys Phe Gln 85 90 95 Glu Glu Met Asp Lys Val Met Lys Asp Pro Tyr Lys Val Val Met Lys
100 105 110 Gln Ser Lys Leu Pro Met Ser Leu Leu His Asp Arg Ile Gln Pro His 115 120 125 Asn Ala Lys Val His Ile Leu Asp Thr Glu Ser Phe Glu Ser Thr Phe Gly Pro Lys Ser Gln Arg Lys Arg Pro Asn Leu Phe Ala Ser Asp Met 145 150 155 160 Gln Ser Leu Leu Glu Asn Ala Glu Met Ser Thr Glu Ser Tyr Asp Gln 165 170 175Gly Lys Asp Arg Asp Leu Val Met Glu Asp Thr Gly Val Arg Asn Glu 180 185 190 Ala Gln Glu Glu Ile Tyr Lys Lys Gly Gln Ser Lys Arg Ile Trp Gly
195 200 205 Glu Leu Tyr Lys Val Ile Asp Ser Ser Asp Val Val Gln Val Leu 210 215 220 Asp Ala Arg Asp Pro Met Gly Thr Arg Ser Pro His Ile Glu Ala Tyr 225 230 235 240 Leu Lys Lys Glu Lys Pro Trp Lys His Leu Ile Phe Val Leu Asn Lys 245 250 255 Cys Asp Leu Val Pro Thr Trp Ala Thr Lys Arg Trp Val Ala Val Leu 260 265 270 Ser Gln Asp Tyr Pro Thr Leu Ala Phe His Ala Ser Leu Thr Asn Pro 275 280 285

Phe Gly Lys Gly Ala Phe Ile Gln Leu Leu Arg Gln Phe Gly Lys Leu 290 295 300 His Thr Asp Lys Lys Gln Ile Ser Val Gly Phe Ile Gly Tyr Pro Asn 305 310 315 320 Val Gly Lys Ser Ser Val Ile Asn Thr Leu Arg Ser Lys Lys Val Cys 325 330 335 Asn Val Ala Pro Ile Ala Gly Glu Thr Lys Val Trp Gln Tyr Ile Thr 340 345 350 Leu Met Arg Arg Ile Phe Leu Ile Asp Cys Pro Gly Val Val Tyr Pro 355 360 365 Ser Glu Asp Ser Glu Thr Asp Ile Val Leu Lys Gly Val Val Gln Val 370 375 380 Glu Lys Ile Lys Ala Pro Gln Asp His Ile Gly Ala Val Leu Glu Arg 385 390 395 400 Ala Lys Pro Glu Tyr Ile Ser Lys Thr Tyr Lys Ile Glu Ser Trp Glu
405 410 415 Asn Ala Glu Asp Phe Leu Glu Lys Leu Ala Leu Arg Thr Gly Lys Leu 420 425 430 Leu Lys Gly Glu Pro Asp Met Leu Thr Val Ser Lys Met Val Leu 435 440 445 Asp Trp Gln Arg Gly Arg Ile Pro Phe Phe Val Lys Pro Pro Asn 450 455 460 Ala Glu Leu Pro Thr Asp Ser Gln Leu Pro Pro Ser Ser Pro Leu Glu 465 470 475 480 Val Pro Thr Glu Thr Thr Gln Asn Asn Pro Glu Glu Glu Thr Thr Glu 485 490 495 Thr Glu Val Glu Arg Ser Asp Ser Ile Thr Glu Lys Glu Pro Glu Gly 500 510 Asp Cys Ser Gln Asp Arg Asn Ser Glu Met Gln Gln Ile Leu Ala Arg 515 520 525 Val Arg Gln Asn Phe Gly Lys Ile Asn Val Gly Pro Gln Phe Ser Ala 530 540

Asp Asp Leu Val Pro Val Glu Met Ser Asp Leu Glu Asp Leu Glu Ser 545 550 555 560 Ser Gly Glu Glu Glu Gln Glu Gln Glu Gln Pro Gly Glu Asp Ala 565 570 575 Glu Glu Glu Arg Ser Pro Asp Thr Gln Glu Glu Pro Val Gly Asn Asp 580 585 590 Thr Lys Ala Val Leu Arg Ala Leu Asp Glu Lys Ile Ala Lys Tyr Gln 595 600 605 Phe Leu Asn Lys Ala Lys Ala Lys Lys Phe Ser Ala Val Arg Ile 610 620 Ser Lys Asp Leu Ser Glu Lys Val Phe Ala Lys Tyr Lys Glu Glu Lys 625 630 635 640 Lys Thr Ser Ala Glu Asp Ser Asp Ala Ala Pro Thr Lys Lys Ala Arg 645 650 655 Lys Trp Asp Ala Gln Met Glu Glu Glu Pro Ser Asn Lys Thr Gln Arg 660 665 670 Met Leu Thr Cys Lys Glu Arg Arg Arg Ala Ala Arg Gln Gln Gln Ser 675 680 685 Lys Lys Val Gly Val Arg Tyr Tyr Glu Thr His Asn Val Lys Asn Arg 690 695 700 Asn Arg Asn Lys Lys Lys Thr Ser Asp Ser Glu Gly Gln Lys His Arg 705 710 715 720 Arg Asn Lys Phe Arg Gln Lys Gln 725